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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/489,394	01/21/2000	Vanessa Hsei	P1085R6	5782
9157	7590	09/27/2004	EXAMINER	
GENENTECH, INC. 1 DNA WAY SOUTH SAN FRANCISCO, CA 94080			HELMS, LARRY RONALD	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/489,394

**Applicant(s)**

HSEI ET AL.

**Examiner**

Larry R. Helms

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 124-132 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 124-132 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. Claims 1-123 have been canceled.  
Claims 126-127, 132 have been amended.
2. Claims 124-132 are pending and under examination..
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

### ***Specification***

4. The specification is objected to for the following reason:
  - a. The first line of the specification needs to be updated to indicate the proper relationship between the applications being claimed under 35 USC 120. For example a CON, CIP, DIV. It is noted that it appears that applications 09/355014, 08/804444, 09/012,116, 09/026985 are all CIPs of the instant application (see Priority below).

### ***Rejections Withdrawn***

5. The rejection of claim 126 and 127 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

### ***Response to Arguments***

6. The rejection of Claims 124-132 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 20, 25, 26, 28, 31, 32-36 of copending Application No. 09/726,258 in view of Carter et al (Antibody Engineering, A practical approach, IRL Press, chapter 13, pages 291-308, 1996, IDS #8) and Allan et al (U.S. Patent 5,620,689, filed 6/95) is maintained.

The response filed 7/15/04 (5/3/04) has been carefully considered but is deemed not to be persuasive. The response states that as these rejections are provisional, applicants await an indication of allowable subject matter at which time a determination of whether common subject matter has been claimed and to the suitability of a TD may be assessed. In response to this argument, no TD has been filed and as such the rejection is maintained.

7. The rejection of claims 124-132 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 27 of copending Application No. 09/355,014 in view of Carter et al (Antibody Engineering, A practical approach, IRL Press, chapter 13, pages 291-308, 1996, IDS #8) and Allan et al (U.S. Patent 5,620,689, filed 6/95) is maintained.

The response filed 7/15/04 (5/3/04) has been carefully considered but is deemed not to be persuasive. The response states that as these rejections are provisional, applicants await an indication of allowable subject matter at which time a determination of whether common subject matter has been claimed and to the suitability of a TD may

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be assessed. In response to this argument, no TD has been filed and as such the rejection is maintained.

***Priority***

8. It is noted that the priority has been updated in this application. The priority has been changed to add US applications 09/355014, 08/804444, 09/012,116, and 09/026985 and provisional applications 60/038664 and 60/074330. Upon review of all of these applications no support for a conjugate of an antibody that binds VEGF, HER2, CD20, CD18, CD11a, human IgE, human apo-2 receptor, TNF-alpha, TF, human integrin, EGFR, CD3, TAC (essentially all binders that are claimed in the Markush group in claim 1) is seen in any of these applications. Support is seen in the instant application and in the provisional application 60/116787, filed 1/21/99. As such the claims are granted the priority of 1/21/99.

9. The rejection of claims 124-130 under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al (U.S.Patent 6,133,426, priority to 1/22/98) and further in view of Zapata et al (FASEB J. 9:A1476, 1995, IDS #8) is maintained.

The response filed 7/15/04 (5/3/04) has been carefully considered but is deemed not to be persuasive. The response states that the claims get priority to the 08/804444 application filed 2/21/97 so Gonzales is not prior art even if it were not a priority document (see page 7 of response). In response to this as stated above the claims get

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the priority of 1/21/99 and as such Gonzales is prior art. The response further states Zapata discusses that nonspecific clearance of an antibody Fab fragment with a molecular weight of 49 kD can be decreased by addition of a 10 kD PEG and as long as the effective molecular size is below 70 kD clearance decreases as molecular weight increases and as such Zapata does not make obvious the present claims (see page 8 of response). In response to this argument, Zapata does not mention anything about nonspecific clearance or molecular weights of 49 kD or 70 kD. It is unclear what this argument has to do with the art of Zapata.

10. The rejection of claims 124-130 under 35 U.S.C. 103(a) as being unpatentable over Faanes et al (U.S. Patent 5,695,760, filed 4/24/95, IDS #8) and further in view of Zapata et al (FASEB J. 9:A1476, 1995, IDS #8) and Braxton (US Pat. No. 5,766,897, IDS #8) is maintained.

The response filed 7/15/04 (5/3/04) has been carefully considered but is deemed not to be persuasive. The response states Zapata has been described above. In response to this the discussion above applies to the Zapata reference. The response further states that Faanes discusses full-length antibodies and not fragments and does not suggest a molecular weight of at least about 500 kD and Applicants have unexpectedly found that conjugation of nonproteinaceous polymers to antibody fragments leads to an increase in apparent molecular weight so that conjugation of 20 kD polymer leads to an apparent molecular weight of 500 kD on size exclusion chromatography (see page 9-10 of response). In response to this argument, Faanes

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discusses the antibody can be fragments of antibodies such as Fab and F(ab)<sub>2</sub> (see column 10, lines 12-13) and Faanes also realized that adding PEG to an antibody leads to an increased apparent molecular weight as taught on column 19, lines 23-41. Thus, if the antibody has an increased in apparent molecular weight it would have been obvious that fragments would also have an increased apparent molecular weight with the PEG added. Therefore, it is not surprising or unexpected. The response further states that Braxton does not discuss molecular weight or provides motivation to conjugate 20 kD PEG (see page 9 of response). In response to this argument, Braxton clearly provides motivation to use 20kD PEG with smaller proteins as would be done for antibody fragments which are smaller than intact antibodies.

11. The rejection of claims 124-132 under 35 U.S.C. 103(a) as being unpatentable over Faanes et al (U.S. Patent 5,695,760, filed 4/24/95, IDS #8) in view of Zapata et al (FASEB J. 9:A1476, 1995, IDS #8) and Braxton (US Pat. No. 5,766,897, IDS #8) as applied to claims 124-130 above and further in view of Carter et al (Antibody Engineering, A practical approach, IRL Press, chapter 13, pages 291-308, 1996, IDS #8) and Allan et al (U.S. Patent 5,620,689, filed 6/95) is maintained.

The response filed 7/15/04 (5/3/04) has been carefully considered but is deemed not to be persuasive. The response states that Faanes, Zapata, and Braxton have been described above and Carter and Allan do not make up for the deficiencies. In response to this argument, the response above to Zapata, Faanes, and Braxton applies and Carter and Allan make up for the lack of teachings of HER2 and CD20.

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12. The rejection of claims 124-132 under 35 U.S.C. 103(a) as being unpatentable over Koumenis et al (Protein Science 7(suppl.1):73 7/1998) and further in view of Carter et al (Antibody Engineering, A practical approach, IRL Press, chapter 13, pages 291-308, 1996, IDS #8) and Allan et al (U.S. Patent 5,620,689, filed 6/95) is maintained.

The response filed 7/15/04 (5/3/04) has been carefully considered but is deemed not to be persuasive. The response states that Koumenis is not a proper reference in view of the priority of 2/21/97 (see page 12 of response). In response to this argument, the priority date for the claims are 1/99. The response further states Koumenis lacks a discussion of attachment of a nonproteinaceous polymer to a free sulfhydryl group of cysteine within the hinge (see page 12 of response). In response to this argument, Koumenis teach PEG to Fab' or F(ab)'<sub>2</sub> using sulfhydryl-specific chemistry which in view of Carter who teaches Fab'-SH and attachment of PEG to fragments, it would have been obvious to add the PEG to a hinge cysteine because that is where the cysteine is in the Fab'-SH (see page 301-303 of Carter).

### ***Conclusions***

13. No Claims are allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectfully,


Larry R. Helms Ph.D.

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LARRY R. HELMS, PH.D  
PRIMARY EXAMINER